APPLN. FILING DATE: OCTOBER 9, 2001

TITLE: BILE-ACID CONJUGATES FOR PROVIDING SUSTAINED

SYSTEMIC CONCENTRATIONS OF DRUGS

INVENTOR(S): CUNDY, ET AL.

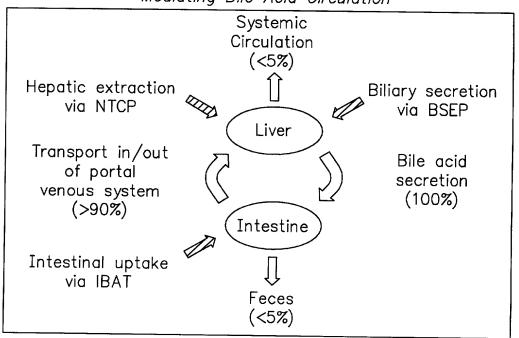
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FIG. 1

FIG. 2The Enterohepatic Circulation with Key Transporter Proteins
Mediating Bile Acid Circulation



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FIG. 3

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Bile Acid Conjugates of HMG-CoA Reductase Inhibitor

FIG. 5

FmocNH
$$CO_2H$$
 (10)

1. CICO₂Et/NEt₃

3. DBU/DMF

H₂N | 0 (1

(8)
$$\frac{1. CICO_2Et/NEt_3}{2. H_2N} CO_2H$$
(3)

HO (12)

3. NaOH/MeOH

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3/5 CO2H NH2 3 1. CICO2Et/NEt3 $\widehat{\mathbf{E}}$ 3. NaOH/MeOH ΙŹ ェ 0 (d6)ভ H છOH R=H © Ξ 工 Also synthesized from ursodeoxycholic acid: F/G. 4 I (96) 1. CICO2Et/NEt₃ $\widehat{\mathbb{C}}$ 0= (ae) 6) HO.,, 9 H0,,,,,

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1. CICO₂Et/NEt₃

FIG. 7

$$H_2N$$
 H_2N
 H_2N
 H_3N
 H_4N
 H_5N
 H_5N

FIG. 8

(22)
$$\frac{1. 2,4,6-CI_3C_6H_2C(0)CI}{Et_3N, DMAP}$$

2. TFA

3. Na⁺ exchange resin H₂O/MeOH

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